

Bioassay, carcinogenesis and tissue culture

#230R1

Committee:

Drs. Jacobson, Chm.  
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Originally activated  
Feb. 1, 1960

TOBACCO INDUSTRY RESEARCH COMMITTEE  
150 East Forty Second Street  
New York 17, N.Y.

Application For Renewal of Research Grant

Date: October 31, 1960

1. Name of Investigator: H. R. Pratt-Thomas, M.D.
2. Title: Professor & Chairman of the Department of Pathology
3. Institution & Address: Medical College of South Carolina  
16 Lucas Street, Charleston, South Carolina
4. Project or Subject: Carcinogenesis in the Laboratory Animal: A comparison of species response to standardized sites of application.
5. Detailed Plan of Procedure:

A towering edifice of experimental data relative to animal carcinogenesis has been constructed over the years, but whether this edifice is structurally sound, particularly in regard to its human application is open to question. The mouse and the rat have been the prime targets in these investigative efforts and the skin and subcutaneous tissues the favorite sites of endeavor. After a decade of working with mice as test animals in an attempt to evaluate the possible carcinogenic effects of smegma and tobacco tars, it has become apparent that the murine cellular response is very labile (specifically as regards cervical and vaginal epithelium) and that a variety of stimuli of relatively innocuous proportions are capable of producing neoplasms e.g. simple trauma and as supported by the following:

Previous Publications:

Heins, Henry C., Dennis, E.J., and Pratt-Thomas, H.R.: The Possible Role of Smegma in Carcinoma of the Cervix. Amer. Jour. Obs. and Gyn. 76:726-735, October, 1958.  
Pratt-Thomas, H.R., Heins, H.C., Latham, E., Dennis, E.J., and McIver, F.A.: The Carcinogenic Effect of Human Smegma: An Experimental Study. Part I: Preliminary Report. Cancer, 9:671-680, July-Aug., 1956. Also Biologic Assay of Cigarette Smoke Tars (to be published).

As the premise of carcinogenic effect in man is often supported by such evidence as the production of neoplasms in the laboratory animal, it is extremely important that species variations be taken into consideration so that any carcinogenic effects may be placed in their true perspective.

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5. Detailed Plan of Procedure (continued-page 2)

We propose to utilize groups of different laboratory animals, rabbits, mice, guinea pigs, hamsters, and rats (monkeys also desirable, but expensive and definitely require long term exposure) and to expose each group to identical agents by means of the same procedures. We would utilize chiefly intra-vaginal application technique with which we have had a great deal of experience, but plan to use skin and subcutaneous areas as well so that we may employ a greater range of substances without increasing the number of animals to impractical proportions. The agents to be used would include some of the patent polycyclic hydrocarbons, but particular attention would be given to such agents as ethyl alcohol, silver nitrate, para-formaldehyde, simple trauma, xylene, etc. The impression has been gained that mice (at least some strains) will react in a neoplastic fashion to a wide variety of stimulating or irritating agents, provided the stimulus is applied for a sufficient length of time.

Report of Progress

It has been possible to obtain inbred strains of mice, rats, hamsters and guinea pigs.

One hundred and forty animals have now been committed to the experiment consisting of 30 mice, 50 rats, 30 hamsters and 30 guinea pigs. The animals have been divided into groups of ten and at the present time intravaginal application of the following substances are applied to the cervices twice weekly: 1% 3-4 Benzpyrene 15% 8-hydroxyquinoline, 1% tobacco tar concentrate. These materials have all been mixed in #1500 carbowax. We propose by January 1, 1961 to also utilize some unusual fatty acids obtained from various strains of mycobacteria as well as tryptophan metabolites. These will be utilized for intravaginal application and will, also along with the substances previously mentioned, be injected into the subcutaneous areas of these animals. Only a single subcutaneous injection of the material is contemplated at present. These materials have been chosen not only to test and compare the species response as originally proposed but also to possibly shed light on the problem of carcinogenesis in regards to chemical agents which we and other groups of investigators are studying.

6. Budget Plan:

a. Salaries	\$7000.00
b. Expendable Supplies	700.00
Permanent Equipment	300.00
Overhead (15% of a + b)	1155.00
Other	-----
	\$ 9155.00

7. Anticipated Duration of Work: 3 years.

8. Facilities and Staff Available: H. R. Pratt-Thomas, M.D. - Principal Investigator. No salary. R. R. Steuer, M.D. - Research Fellow in Pathology. James McInnes, Mack Davis and Ralph Mollycheck-Student Assistants. Frank Nelson-Diener. Miss Mildred Goddard-Technician.

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8. Facilities and Staff Available: (Continued)

A first class temperature controlled animal room with proper equipment is in use. All technical pathology equipment is available and being utilized. Sufficient personnel to make the injections and properly care for these somewhat temperamental animals is the major item of expense.\*

9. Additional Requirements:

Cages. See above.

10. Additional Information (Including relation of work to other projects and other sources of supply):

The publication of the U.S. Department of Health, Education, and Welfare "Survey of Compounds which have been tested for Carcinogenic Activity" Supplement 1, 1957 lends support to some of the proposals and ideas expressed in the formulation of this project. The numerous articles dealing with animal carcinogenesis and the implication, directly or indirectly inferred, of its relation to neoplastic disease in man makes clarification of this problem mandatory.

/s/ H. R. Pratt-Thomas, M.D., Director of Project

/s/ L. W. Michaelis, Business Officer of the  
Institution

\* The cost has increased slightly from last year because of the number of animals being utilized and because a few additional cages are necessary.

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